PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
SASTRY *et al.*

Serial No.: 08/869,386

Filed: 06/05/97

For: COMPOSITIONS AND METHODS FOR ELICITING AN IMMUNE RESPONSE

Group Art Unit: 1648

Examiner: B. Nelson

Atty. Dkt. No.: UTXC:538/HYL

CERTIFICATE OF MAILING
37 C.F.R. 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date below:

09/15/99
Date

Steven L. Highlander

DECLARATION OF DR. RALPH B. ARLINGHAUS UNDER 37 C.F.R. §1.132

Hon. Assistant Commissioner for Patents
Washington, D.C. 20231

I, Ralph B. Arlinghaus, declare that:

1. I am the Ralph B. Arlinghaus named as an inventor on the above-captioned application. I currently hold the position of Professor and Chairman in the Department of Molecular Pathology at the University of Texas M. D. Anderson Cancer Center, Houston, Texas.

2. It is my understanding that, in an Office Action dated April 16, 1999, the examiner has rejected claims 29-47 as lacking enablement under 35 U.S.C. §112, first paragraph. More

specifically, the examiner believes that the specification does not enable a method of inhibiting HIV entry into cells *in vivo*.

3. In order to ascertain the *in vivo* efficacy of the R15K peptide, a chimpanzee HIV-challenge experiment was performed. Prior to the *in vivo* experiment, an *in vitro* study was performed where PMBCs from three chimpanzees were infected with HIV-1 IIIB. Low levels of infection were established in these cells. Administration of R15K peptide to the PMBCs inhibited this low level of infection altogether. *In vivo* experiments involved infection of all three animals with HIV-1 IIIB. Two of the animals were treated with R15K peptide, each receiving a total of 8 injections by intravenous infusion over a 28-day period. The third animal served as a negative control and did not receive any R15K. Virus titer was monitored at various time points using quantitative PCR™.

4. The *in vitro* infection experiments demonstrated that R15K administration eliminated the infection in chimpanzee PMBCs. In the *in vivo* experiments, for the two chimpanzees treated with R15K peptide, 4 of 7 samples taken during the 28-day treatment period were negative for virus, while the other 3 samples were positive, but only at low levels. Scoring degree of positive per sample gives a value of 0.43. On the other hand, for the negative control animal, out of a total of 4 samples examined, 3 showed positive counts with two showing substantial amounts of virus. Again, degree of positive per sample gives a value of 1.38, more than triple that of the treated animals.

Evidence for Medical Utility of R15K in a Chimpanzee Animal Model:

DAY	R15K Infusion	PCR™-Results Chimpanzee #124 (R15K-treated)	PCR™-Results Chimpanzee #129 (R15K-treated)	PCR™-Results Chimpanzee #139 (negative-control)
0	+	-	-	-
1	+	ND	ND	ND
3	+	-	-	+/-
7	+	+	+	2+
11	+	ND	ND	ND
14	+	+	-	-
21	+	ND	ND	ND
28	+	-	ND	3+
41	-	ND	ND	ND
69	-	-	-	-
83	-	-	4+	2+
111	-	-	-	-

*Chimpanzees 124 and 129 were injected with R15K. Chimpanzee 139 was not. All three chimpanzees were inoculated with HIV virus. Chimpanzees were infected at day 1. The viral strain was adapted for replication in chimpanzees. ND= no data; - = negative; + = positive.

5. These results suggest that the R15K peptide inhibits HIV replication *in vivo* in chimpanzees. It is known that HIV-replication exhibits periodicity in chimpanzees, which is reflected by the variability in results for a given animal. However, the overall titers during the test period clearly were higher in the untreated animal, as compared to the R15K-treated animals.

6. I hereby declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

8/19/99
Date

Ralph B. Adlinghaus
Ralph B. Adlinghaus, Ph.D.